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Obesity Comorbidity/Lifestyle Intervention

A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety

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Summary

Obesity is a rising problem, especially among women of reproductive age. Overweight and obesity reduce both physical and mental health. Lifestyle interventions could have beneficial effects on both, but an overview of the effects on mental health, especially in women of reproductive age, is currently lacking. Therefore, the aim of this review was to assess the effect of lifestyle interventions on symptoms of depression and anxiety in women of reproductive age with overweight or obesity. The databases MEDLINE, EMBASE and PsycINFO were searched from inception to June 2018 for published randomized controlled trials (RCTs). We included lifestyle intervention RCTs in women of reproductive age with overweight or obesity that assessed effects on symptoms of depression and/or anxiety. The difference between baseline and post-intervention scores on symptoms of depression and anxiety for the intervention and control group was analysed. Meta-analysis was performed with a random effects model.* The search resulted in 5,316 citations, and after screening five RCTs were included, in which 571 women were randomized. The effect of lifestyle interventions on depression scores was investigated among 224 women from five RCTs. The pooled estimate for the mean difference was -1.35 (95% CI, -2.36 to -0.35 , $p = 0.008$). The effect of lifestyle interventions on anxiety levels was studied among 148 women from four RCTs, resulting in a pooled estimate of -1.74 (-2.62 to -0.87 , $p < 0.001$). Based on five RCTs, meta-analyses showed that lifestyle interventions in women of reproductive age with overweight or obesity consistently reduce symptoms of depression and anxiety.

Keywords: Anxiety, depression, lifestyle intervention, obesity.

Abbreviations: BMI, body mass index; RCT, randomized controlled trial; CI, confidence interval; GWB, general well-being; CESD, Center of Epidemiological Studies Depression; STAI, Spielberger State-Trait Anxiety Inventory; POMS, Profile of Mood States.

*The protocol was registered in PROSPERO (CRD42015020902).

Introduction

Obesity is increasing worldwide at an alarming rate, with an exceptionally strong rise among women of reproductive age (1,2). Obesity does not only reduce physical health, but mental health as well (3–6); it is associated with depression and suicidal behaviour (7). Individuals affected by obesity have a 20–50% higher prevalence of major depressive disorders (7) and more anxiety (8). Also, depression and comorbid anxiety are associated with weight gain suggesting a bidirectional relationship (9).

The relationship between obesity and major depressive disorder is different for men and women. While major depressive disorder is associated with a high body mass index (BMI) in women, it is associated with lower BMI in men (10). Unlike men, young women with overweight or obesity are more likely to have experienced depressive symptoms than women with normal weight, and they are also more likely to have sustained depressive symptoms (11). Furthermore, the U-shaped association between BMI and anxiety among women is not found in men (12).

International guidelines advise lifestyle modification as the first step in treatment of overweight and obesity (13). Lifestyle interventions have been demonstrated to be effective in improving cardiometabolic health, quality of life and body image (14–16). The effects of lifestyle interventions on symptoms of depression have been studied extensively, but primarily in middle to late aged men and women (15,17,18). The psychological effects of lifestyle interventions in younger women are largely unknown. Research in this population would be a relevant addition to the existing evidence regarding the effectiveness of lifestyle interventions, especially since obesity and overweight are so prevalent in young women (19). Furthermore, in a population of women of reproductive age where depression and anxiety are relatively frequent, the use of an effective lifestyle intervention might lead to a greater reduction of burden of disease in the population. Additionally, relatively young women may consider their (future) role as a parent, and be more receptive to lifestyle advice, in order to be good role models (20). Moreover, decreasing symptoms of depression and anxiety after a lifestyle intervention in women before pregnancy could hypothetically improve the intrauterine environment and improve the health of the offspring, since maternal depression is associated with offspring inflammation in adult age (21).

Symptoms of depression and anxiety are important outcomes for patients, and a reduction in these symptoms could prevent future weight gain (22). Yet, the effect of lifestyle interventions in women of reproductive age on symptoms of depression and anxiety has not been addressed in a systematic review.

Therefore, the aim of this systematic review was to summarize existing evidence from randomized controlled trials (RCT) comparing the effects of a lifestyle intervention to a control condition on symptoms of depression and anxiety in women of reproductive age with overweight or obesity.

Methods

Literature search

The review protocol with the exact search strategy and inclusion and exclusion criteria was published in 2015 in PROSPERO, an online registry for systematic reviews (number CRD42015020902). The databases MEDLINE, EMBASE and PsycINFO were searched for published studies from inception to June 2018. The search strategy consisted of controlled and free text terms for the patients (female, overweight or obesity), the intervention (lifestyle intervention, behavioural therapy, diet, exercise, weight loss), the outcome (depression, anxiety, mental health) and the type of study (RCT). Publications in English, Dutch or German were considered. A total of 5,316 publications were identified in the database searches (MEDLINE = 2,303, EMBASE = 2,236, PsycINFO = 777). After excluding 608 exact and 579 close duplicates (close duplicates are two very similar records, that require extra inspection), 4,129 publications were eligible for title and abstract screening. The PRISMA guidelines were used for the reporting in this systematic review.

Study selection

Randomized controlled trials reporting on depression and/or anxiety levels, in women of reproductive age with overweight or obesity (BMI > 25), were eligible for inclusion in this systematic review. Reproductive age was defined as the period from menarche until menopause, or age between 19 and 55 years. In the protocol registered in PROSPERO, the age range was defined as 19 to 44 years of age; this was adjusted up to 55 years of age in order to capture all studies examining women of reproductive age. Studies were excluded if the study was not a RCT, if the full-text article was not in English, Dutch or German, if the population did not consist of women of reproductive age, if the intervention was not aimed at weight loss or if the intervention consisted of pharmacological treatment, or if the study included only women with a diagnosis of prior (mental) disease. The last exclusion criterion was chosen because people with (mental) illness have different anxiety and depression levels compared with people without (mental) illness (23). Furthermore, the control group may have received an information folder about weight loss but could not have participated in a lifestyle

intervention. Study protocols, conference abstracts and dissertations were also excluded.

The study selection was done in Covidence (www.covidence.org), which is an online application in which two authors (L.vD. and V.W.) could independently screen on title, abstract and full text, without information about each other's selections.

Data extraction

Double data extraction was performed by L.vD. and V.W. The following information was extracted in a standardized data collection form in Covidence: country, study setting, inclusion and exclusion criteria, number of participants, baseline characteristics, description of the intervention program and control strategy, depression and/or anxiety questionnaire, weight loss and reduction in depression and/or anxiety symptom levels.

Quality assessment

The quality of included studies was assessed twice by L.vD. and V.W. with the Risk of Bias tool from the Cochrane Collaboration. Conflicts were resolved by discussion (24). The Risk of Bias instrument rates the following domains: sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessors (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias) and other sources of bias. The answer categories to evaluate the bias are high risk, low risk and unclear.

Statistical analysis

The difference between baseline and post-intervention scores on depression and/or anxiety questionnaires for the intervention and control group was analysed. Heterogeneity was assessed with the standard Chi-square (significance level: 0.1) and I-squared (75–100% interpreted as considerable heterogeneity) statistics. The I-squared statistic measures the proportion of the variance that can be accounted for by true differences in effect size. Pooled data were analysed with a random effects model in Review Manager (RevMan 5.3). A random effects model was chosen because the goal was not to estimate one true effect size, but to estimate a mean of a distribution of effect sizes. Results are presented as standardized mean differences and 95% confidence intervals (CI) and shown in forest plots. If the same questionnaire was used to assess symptoms of depression and anxiety in different studies, the mean difference was reported.

Results

Study characteristics

A total of 4,129 unique publications were eligible for title and abstract screening. After eliminating publications because of language, type of study design (e.g. cohort, case-control, quasi-experimental), lack of control group, type of population, absence/lack of lifestyle intervention and the lack of psychological outcomes, 118 full text publications were considered for this systematic review. Of these publications, 113 were not suitable because the study population was not restricted to women of reproductive age (49 publications) or symptoms of depression or anxiety were not reported (26 publications), or because of other reasons (38 publications) as described in Fig. 1. The study selection process, which led to a total of five studies that were suitable for this meta-analysis, is described in Fig. 1. Table 1 shows the characteristics of the five studies included in this systematic review, which were all community-based RCTs performed in the USA or UK. Overall, 571 women with overweight or obesity were included, of whom 301 intervention, and 270 control participants, with a mean age ranging from 34.2 to 41.2 years. The intervention duration varied from 12 weeks to 1 year. Five studies assessed symptoms of depression (25–29) and four of them assessed symptoms of anxiety (25–27,29) after a lifestyle intervention.

Symptoms of depression and anxiety were assessed with the general well-being (GWB) questionnaire in three studies (25–27); this questionnaire has demonstrated good validity and psychometric properties (30). One study (28) used the Center for Epidemiological Studies Depression (CESD) scale to measure symptoms of depression, with extensive support for its validity and reliability (31). Symptoms of depression were measured with the Profile of Mood States (POMS) in the last study (29). This questionnaire has also shown solid internal consistency and validity (32). In this study, symptoms of anxiety were measured with the Spielberger State-Trait Anxiety Inventory (STAI), which was also validated in previous research (33). None of these questionnaires can distinguish symptoms from disorders in a reliable manner and thus cannot be used to diagnose but rather to assess symptoms. Previous research regarding measurement of depression symptoms suggested the POMS and CESD questionnaire are highly correlated (34). Another study reported improvement in GWB depression scores after a lifestyle intervention, but no improvement in POMS depression scores, which could be due to lower sensitivity to detect changes in healthy adults (35). Symptoms of anxiety measured by different questionnaires, including the GWB and STAI were strongly correlated, except the STAI (36). The GWB might measure general distress, whereas the STAI focusses more on emotional responses and anxiety as a personality characteristic.

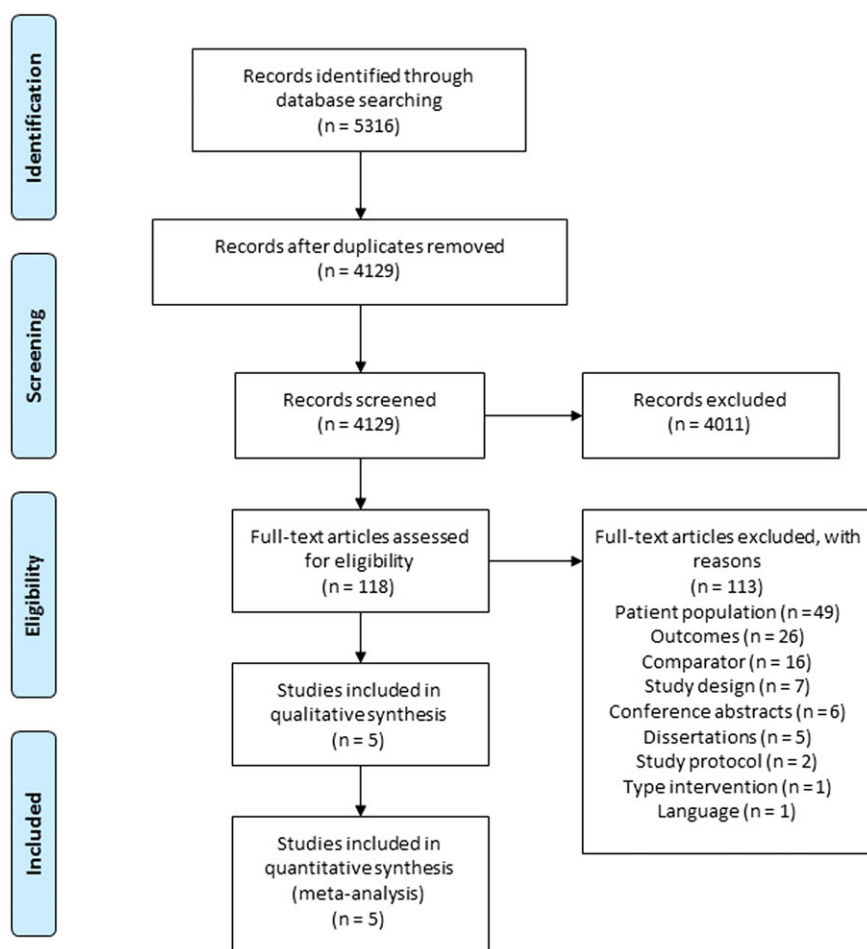


Figure 1 Flow diagram of the study selection process. [Colour figure can be viewed at wileyonlinelibrary.com]

Risk of bias

Table 2 shows the risk of bias assessment for all five studies included in this systematic review. All studies provided minimal information about potential selection bias: Information about random sequence generation and allocation concealment was missing in all studies, which resulted in labeling the risk of selection bias as 'unclear'. One study scored high on reporting bias, since not all outcomes were reported. This study also scored high on attrition bias, since the attrition rate was over 20% (28).

Depression after lifestyle intervention

Five studies (25–29) investigated the effect of a lifestyle intervention on depression symptom scores among 224 participants (Fig. 2). The pooled estimate for the standardized mean difference in depression symptom score rendered from a random effects model was -1.35 (95% CI, -2.36 to -0.35 , $p = 0.008$). The studies showed considerable heterogeneity ($\text{Chi}^2 = 40.19$, $I^2 = 90\%$, $p < 0.001$). Two studies

that included on average younger participants and women with less severe overweight or obesity (27,29), were excluded in a sensitivity analysis. This resulted in a pooled estimate of -2.12 (95% CI, -2.93 to -1.32 , $p < 0.001$), with moderate heterogeneity ($\text{Chi}^2 = 6.49$, $I^2 = 69\%$, $p = 0.04$).

Anxiety after lifestyle intervention

Four studies (25–27,29) investigated the effect of a lifestyle intervention on levels of anxiety symptoms among 148 participants (Fig. 3). The pooled estimate for the standardized mean difference in anxiety symptom score rendered from a random effects model was -1.74 (-2.62 to -0.87 , $p < 0.001$), with considerable heterogeneity ($\text{Chi}^2 = 14.33$, $I^2 = 79\%$, $p = 0.002$). One study measured symptoms of anxiety with a different questionnaire compared with the other studies (29), and if this study was excluded in a sensitivity analysis the mean difference was -3.26 (-4.13 to -2.39 , $p < 0.001$), without considerable heterogeneity ($\text{Chi}^2 = 4.37$, $I^2 = 54\%$, $p = 0.11$).

Table 1 Characteristics of the studies included in the meta-analysis

Author & year	Country	Study design	Population	Age	Questionnaire	Intervention strategy	Control strategy	Weight change in kg, mean (SD)
Borkles 2016 (23)	UK	RCT	Pre-menopausal, predominantly white, females with morbid obesity (BMI ≥ 35)	24–55 years	GWB for depression and anxiety	12 weeks of both lifestyle physical activity and structured supervised aerobic exercise. Healthy eating and weight management sessions with psycho-education were conducted weekly (N = 31)	The waiting list control group was requested to maintain their current lifestyle habits and were scheduled to commence the intensive lifestyle intervention phase after 3 months (N = 31)	Intervention: –3.8 (5.46) Control: 2.9 (6.7) P < 0.05
Carroll 2007 (24)	UK	RCT	Healthy, sedentary, predominantly white, pre-menopausal women with obesity (BMI > 30)	> 18 years	GWB for depression and anxiety	12 weeks non-dieting program with weekly sessions based on self-determination theory to maximize motivation for behavioural change (N = 16)	Waiting list participants were asked to maintain their current lifestyle habits and scheduled to start the intervention phase after 3 months (N = 12)	Intervention: –1.9 (7.75) Control: 2.2 (11.28) P = 0.092
Cramer 1991 (25)	USA	RCT	Premenopausal women with mild obesity (10–40% overweight)	25–45 years	GWB for depression and anxiety	15-week supervised moderate exercise program, with daily training sessions (N = 18)	No program (N = 17)	Intervention: 0 (2.55) Control: 1.8 (3.75) P = 0.001
Kerr 2008 (26)	USA	RCT	Women with a BMI of 25–39	18–55 years;	CESD for depression	Computerized behavioural intervention of 1 year to improve physical activity and nutrition. Tailored support and feedback was provided monthly by e-mail and quarterly by telephone sessions (N = 206)	Usual advice about overweight, and a standard set of materials regarding recommendations for diet and exercise (N = 196)	Not reported
Rippe 1998 (27)	USA	RCT	Women who weighed between 20 and 50% more than the 1983 Metropolitan Life Insurance Table of desirable weight for height	20–49 years	STAI for anxiety and POMS for depression	12 week weight watchers program with a hypocaloric diet, self-selected exercise and education regarding behavior modification techniques. Weekly sessions were facilitated by a trained leader who has lost and is maintaining a healthy weight (N = 30)	Maintain current nutritional practices and physical activity patterns (N = 14)	Intervention: –6.07 (4.01) Control: 1.31 (1.28) P < 0.001

BMI, body mass index; CESD, Center for Epidemiological Studies Depression; GWB, general well-being; POMS, Profile of Mood States; RCT, randomized controlled trial; SD, standard deviation; STAI, Spielberger State-Trait Anxiety Inventory.

Table 2 Risk of bias assessment, a green '+' means low bias, a red '-' means high bias, an empty box means it was unclear if there was high or low bias. [Colour table can be viewed at wileyonlinelibrary.com]

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Borkoles 2016			+	+	+	+	+
Carroll 2007			+	+	+	+	+
Cramer 1991			+	+	+	+	+
Kerr 2008			+	+	-	-	+
Rippe 1998			+	+	+	+	+

Discussion

This systematic review and meta-analysis showed that lifestyle interventions reduce symptoms of depression and anxiety in women of reproductive age with overweight or obesity, although this was based on a limited number of trials including small numbers of women.

The positive effect of lifestyle intervention on symptoms of depression and anxiety in women of reproductive age is

consistent with evidence from studies including middle to late aged men and women (15,37). A systematic review aggregating intervention studies for obesity in adolescents and middle to late aged men and women also showed a decrease in symptoms of depression and anxiety, which was mediated by weight loss (37). In another systematic review and meta-analysis including weight loss studies performed in men and women of all ages, intentional weight loss, including pharmacological interventions, led to reductions in symptoms of depression as well (38), although the reported effects on symptoms of depression were smaller compared with our results. This difference could be attributed to the populations included in the systematic reviews. Young women with overweight or obesity are more likely to have depression and anxiety symptoms, compared with men or women of middle to late age (11,12,39). Because these symptoms are more likely to be present in this population, a greater reduction might be expected in symptoms of depression and anxiety in a young female population with overweight or obesity, after a lifestyle intervention.

The mechanism through which symptoms of depression and anxiety decrease after a lifestyle intervention could be weight loss. In two studies included in the present review, there was significant weight loss in the intervention group, and stable weight or weight gain in the control group. Whether the effect of the intervention on symptoms of depression and anxiety was mediated by weight loss was not examined in these studies. The systematic review and meta-analysis by Fabricatore *et al.*, examining the association between different weight loss methods and symptoms of depression among men and women of all ages, found no relationship between changes in weight and changes in depression symptoms, while a significant reduction was found in symptoms of depression for nearly all interventions (38). Hence, at least weight loss alone cannot explain the reduction in symptoms of depression. Meta-regression analysis could shed light on the mediating effect of weight change on symptoms of depression and anxiety, but we could not perform such an analysis, since the results are not reliable when the number of included studies is low, as was the case in our study (40). Another mediating mechanism through which symptoms of depression and anxiety could decrease are the behavioural strategies used in lifestyle

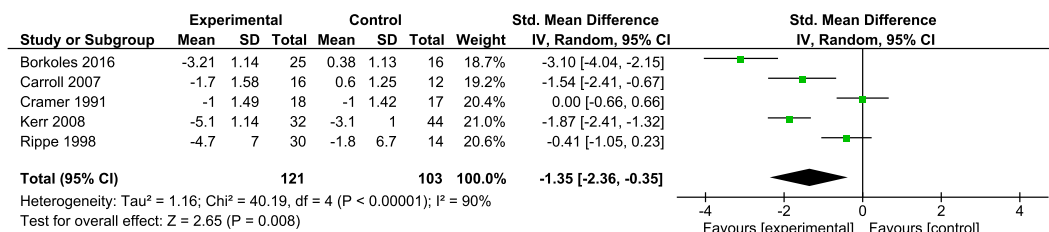


Figure 2 Forest plot assessing the change in depression score between baseline and post-intervention, in the experimental and control group. [Colour figure can be viewed at wileyonlinelibrary.com]

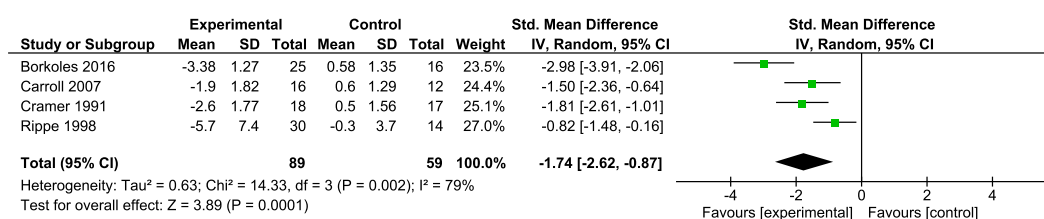


Figure 3 Forest plot assessing the change in anxiety score between baseline and post-intervention, in the experimental and control group. [Colour figure can be viewed at wileyonlinelibrary.com]

interventions. These strategies could reinforce self-acceptance and self-control and decrease the stigma regarding obesity (38). Only one study included in the current meta-analysis did not include a behavioural component in the intervention. Interestingly, this is one of the two studies that found no effect of the intervention on weight loss or depression scores over time, suggesting that a behavioural component in lifestyle interventions is important (27). Changes in lifestyle, including diet and physical activity, were measured in only one of the included studies, which makes summarizing the evidence for these potential mediators not possible. Cramer *et al.* suggested that an improvement in physical fitness is positively correlated with improvement in the total general well-being score. Exercise interventions have shown improvements in depression and anxiety symptoms in a range of studies (41,42), possibly due to changes in serotonin, cortisol and growth factors (42). Besides exercise, diet might mediate the effect of a lifestyle intervention on symptoms of depression and anxiety as well. Previous research indicates dietary patterns may influence the onset of depression (43), although results are mixed and a large longitudinal cohort study reported no association between dietary pattern and depressive symptoms after adjustment for confounding factors (44).

Intervention duration could be another important factor related to the impact of a lifestyle intervention on symptoms of depression and anxiety. In the current meta-analysis, however, the duration of the interventions did not seem to play an important role in the effects on symptoms of depression and anxiety. A previous meta-analysis in males and females of all ages also showed no association between intervention duration and decrease in symptoms of depression (38). Besides the duration, the content and targets of the intervention might also play a role in the impact of a lifestyle intervention on symptoms of depression and anxiety. Future research should investigate the mediating effects of age- and reproductive life phase-related factors, such as body weight after pregnancy in lifestyle interventions.

For a reduction in symptoms of depression, the effect of the interventions was more homogeneous and slightly larger in studies including women with severe obesity and of relative older age (25,26,28). Because severe obesity is associated with greater risk for depression, a larger reduction in symptoms might be expected after a lifestyle intervention

in women with severe obesity, compared with those with overweight or mild obesity.

There are limitations to this systematic review and meta-analysis. First, the low number of studies and limited participant numbers impair the external validity of this meta-analysis. Second, important information regarding the randomization was missing, resulting in an unknown risk of bias, although the total risk of bias was low. It was not possible to present a funnel plot for information regarding publication bias, since funnel plots are not reliable for <10 studies (45). Additionally, depression and anxiety symptoms were measured with various questionnaires, which may have led to different profiles of depression and anxiety. The questionnaires used in the studies included in this meta-analysis measure moderate symptoms of depression and anxiety. The effects are picked up by various questionnaires in a consistent way, and the reduction of symptoms of depression and anxiety after participation in a lifestyle intervention is an important outcome, even if the symptoms are moderate. The total effect size for symptoms of depression after a lifestyle intervention was somewhat larger compared with the previously mentioned meta-analysis of weight loss trials in males and females of all ages (38). However, changes in scores of questionnaires measuring symptoms of depression and anxiety are difficult to interpret in terms of clinical relevance cannot be made. The CESD questionnaire developers have provided a cutoff score ≥ 16 for identifying individuals at risk for clinical depression; compared with this cutoff score, the decrease of approximately 5 points on the CESD score after the intervention suggests this difference is relevant (46). The designs of the lifestyle interventions were heterogeneous; there was variation in the duration of the intervention, the number of intervention sessions and content of the intervention with some interventions only focusing on exercise, other interventions focusing on exercise and diet, and not all interventions included behavioural strategies. Because there were differences in the lifestyle interventions, the effectiveness of different components could be studied. The inclusion of a behavioural component in the intervention may be an important factor in reducing symptoms of depression and anxiety. Information regarding ethnic background and education level was not reported in most studies, and therefore the generalizability of the results from this systematic review

and meta-analysis is unclear. Lastly, no physical and endocrinological examination was performed to confirm premenopausal status in the included studies, which might have resulted in the inclusion of some post-menopausal women in the studies used in the meta-analysis.

There is a need for further studies examining the effects of various lifestyle intervention programs on symptoms of depression and anxiety, so more information becomes available about the most suitable intervention to reduce symptoms of depression and anxiety. The studies included in this systematic review and meta-analysis show consistent reductions in symptoms of depression and anxiety after participation in a lifestyle intervention. However, in the selection process of studies, a large proportion of lifestyle intervention studies was excluded because symptoms of depression or anxiety were not measured. Systematic measurement of symptoms of depression and anxiety in lifestyle intervention trials is recommended to facilitate a better understanding of the implications and effects of lifestyle interventions on both physical and mental well-being.

Conclusion

In this systematic review and meta-analysis, we found that lifestyle interventions in women of reproductive age with overweight or obesity consistently reduce symptoms of depression and anxiety. The beneficial effect of lifestyle interventions on symptoms of depression and anxiety may be mediated by weight loss and putatively by the behavioural strategies used in lifestyle interventions. The reduced symptoms of depression and anxiety after a lifestyle intervention might be especially important for women planning a pregnancy, since this could potentially improve the intrauterine environment and have beneficial effects on health of the offspring. More research is necessary to further unravel the mechanistic paths through which lifestyle interventions decrease symptoms of depression and anxiety. Potential benefits of lifestyle interventions on mental health may not be detected because mental health is not assessed in all lifestyle intervention studies. Therefore, we recommend the systematic measurement of symptoms of depression and anxiety in lifestyle intervention studies.

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Conflicts of interest

The authors report no conflicts of interest.

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